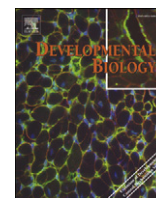


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Concurrent Session 9: Cell and Tissue Polarity

Program/Abstract # 51

An E-Cadherin-mediated hitchhiking mechanism for *C. elegans* germ cell internalization during gastrulation

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Cells that produce internal organs move into the interior of the embryo during gastrulation. Somatic cell gastrulation movements are regulated by transcription factors that also control cell fate, ensuring that cell identity and position are coupled. By contrast, primordial germ cells (PGCs) in many species are transcriptionally quiescent, suggesting that they use alternative strategies to internalize. We show that *C. elegans* PGCs adhere to internal endodermal cells, which undergo morphogenetic movements that pull the PGCs into the embryo. We show that HMR-1/E-cadherin is enriched in PGCs, that HMR-1 is required for PGC internalization and PGC-endoderm adhesion, and that HMR-1 enrichment in PGCs is mediated by the hmr-1 3' untranslated region. Our findings demonstrate the novel strategy that quiescent PGCs use to internalize during gastrulation, and identify a morphogenetic role for the evolutionarily conserved association between PGCs and endoderm.

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Program/Abstract # 52

Gpr125 - a novel planar cell polarity pathway component in zebrafish

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Planar cell polarity (PCP) signaling, initially discovered in *Drosophila* mediates the establishment of polarity within the plane of an epithelium. In vertebrates, an evolutionarily conserved Wnt/PCP pathway has been identified that regulates distinct planar polarized features in various epithelial and mesenchymal cell types. During zebrafish gastrulation, convergence and extension (C&E) movements narrow embryonic tissues dorsoventrally and elongate them antero-posteriorly. Although the Wnt/PCP pathway is a key mediator of C&E, the known components do not fully account for all cell behaviors contributing to C&E. In our search for unknown regulators of zebrafish gastrulation, we have identified Gpr125 as a novel PCP component. As demonstrated for other PCP genes, excess Gpr125 function results in C&E defects. Diminished Gpr125 function exacerbates the defects of PCP component mutants, including trilobite (*tri*)/vang-like2 (*vangl2*), silberblick (*slb*)/wnt11 and landlocked (*llk*)/scribble1 (*scrib1*) in the context of C&E and facial motor neuron migration. In addition, doses of Gpr125 unable to disrupt C&E of wild-type embryos exacerbate

C&E defects in *slb/wnt11* mutants. Intriguingly, Gpr125 promotes localized membrane accumulation of Dishevelled (Dvl), the intracellular molecular hub of Wnt/PCP pathway, in animal pole assays. It suggests that Gpr125 may influence PCP upstream or at the level of Dvl. Future experiments will test for biochemical interactions between Gpr125 and Wnt-PCP components and examine the consequences of Gpr125 dysregulation on cell behaviors during C&E.

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Program/Abstract # 53

Scribble is required for normal lumen morphogenesis in the mammalian lung

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The generation of lumina in the respiratory epithelium is critical for lung function. Aberrant lumen size is a feature of a wide range of lung diseases including cystadenomatoid malformations, pulmonary hypertension and asthma. Lumen formation requires the establishment of close epithelial cell–cell contacts that are maintained as a result of tight junctions, adherens junctions and by intact apical–basal (A/B) polarity. Studies in *Drosophila* have established that Scribble is essential for A/B polarity. In mammals, a role for Scribble (Scrib1) in A/B polarity has not been established but perturbation of Scrib1 leads to defects in planar cell polarity (PCP). Because of these key roles in cell polarity, we sought to determine whether loss of Scrib1 function would affect lung morphogenesis. Our results show that Scrib1 is expressed in tight junctions of lung epithelia. The lungs of the Scrib1 mouse mutant Circletail (*Crc*) are smaller than normal and abnormally shaped with fewer airways. Moreover, many airways lack a visible, 'open' lumen. Molecular markers show altered sub-cellular distribution of adherens and tight junction proteins and perturbation of the cytoskeleton in lung epithelial cells. Consistent with these data, time-lapse imaging reveals reduced cohesion of epithelial cells in forming lung buds and epithelial cyst organization in organotypic culture are severely compromised upon Scrib1 knockdown. A/B polarity appears normal but the PCP pathway is perturbed in Scrib1^{Crc}/*Crc* lungs as shown by altered Rho-GTP levels and abnormal distribution of the PCP proteins Celsr1 and Vangl2. Together, our data reveal that Scrib1 is required for proper lung epithelial arrangement and lumen morphogenesis.

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